REVISTA DO INSTITUTO DE MEDICINA TROPICAL DE SÃO PAULO

JOURNAL OF THE SÃO PAULO INSTITUTE OF TROPICAL MEDICINE

REVIEW

http://doi.org/10.1590/S1678-9946202365040

Generalized tetanus: a pediatric case report and literature review

Melis Deniz [1], **Tugba Erat** [2]

ABSTRACT

Pediatric tetanus is a rare and forgotten disease in countries with high childhood tetanus toxoid vaccination rates. Therefore, the clinical manifestations, treatment and management of this potentially life-threatening disease are not well known. With a literature review and discussion of tetanus management in pediatric patients, we describe a clinical course of a rare and fatal but vaccine-preventable disease, the generalized tetanus, in an adolescent who was successfully treated.

KEYWORDS: Tetanus. Children. Vaccine.

INTRODUCTION

Tetanus is one of the diseases prevented by vaccines and is not transmitted from person to person[1]. As a result of higher childhood tetanus toxoid vaccination rates, tetanus incidence has significantly decreased in recent years. There were 264 tetanus patients and 19 deaths reported in the US between 2009–2017, according to the Centers for Disease Control and Prevention[2]. In the European Union, in 2018, 92 tetanus cases were documented and 48 were confirmed[3]. Nine cases of tetanus were reported in Turkey, in 2020[4]. But in countries where vaccination is insufficient, deaths from tetanus still occur. Tetanus-related deaths were estimated at 56,000 deaths worldwide each year[5]. The disease develops with the penetration of the anaerobe *Clostridium tetani*, common in the soil, into the traumatically injured tissue, producing a neurotoxin[1]. The clinical forms of tetanus are generalized, localized, cephalic, and neonatal[6]. Generalized tetanus is the most frequent and fatal clinical form of tetanus[1]. Herein, we describe an unimmunized patient, a 16-year-old boy, diagnosed with generalized tetanus who was successfully treated.

CASE REPORT

A previously healthy 16-year-old boy injured his right hand while carrying building construction materials made of iron. Ten days after the injury, he arrived at the emergency room with generalized spasms. Upon arrival, he developed a sore throat that progressed to trismus, rigidity of the jaw muscles, and sustained generalized muscle spasms. As the patient was unimmunized, tetanus infection was suspected based on clinical signs and symptoms. Tetanus toxoid vaccine was administered intramuscularly. Since tetanus immune globulin (TIG) was not available in the city, intramuscular equine antitoxin was administered after an intradermal test had been performed. Sufficient doses of equine antitoxin could not be obtained, so human TIG was procured from other hospitals. The patient

[1]Sanlıurfa Training and Research Hospital, Department of Pediatric Infectious Diseases, Sanlıurfa, Turkey

[2]Ankara City Hospital, Department of Pediatric Infectious Diseases, Ankara, Turkey

Correspondence to: Melis Deniz
Sanlıurfa Training and Research Hospital, Department of Pediatric Infectious Diseases, Sanlıurfa Egitim ve Araştırma Hastanesi, Eyyubiye, Sanlıurfa, Turkey

E-mail: mlsdnz@gmail.com

Received: 15 March 2023

Accepted: 3 May 2023

was admitted to the pediatric intensive care unit (PICU) of our hospital, and informed consent was given by the patient's parents.

Upon admission to our PICU, his vital signs were normal, and oxygen saturation was 98% on room air. He had tonic contraction and muscular spasms, dysphagia, trismus, muscular rigidity, and tachycardia. Laboratory studies showed the values for white blood cell count (12,070/μL), hemoglobin (11.5 g/dL), urea (31 mg/dL), creatinine (0.86 mg/dL), c-reactive protein (6.6 mg/L), sodium (138 mEq/L), potassium (4.3 mEq/L), creatine kinase (CK) (1,363 IU/L), calcium (9.7 mg/dL), phosphorus (4 mg/dL), magnesium (1.92 mg/dL), alanine aminotransferase (60.6 U/L) and aspartate aminotransferase (88.2 U/L).

He was given intravenous penicillin G (3 million units intravenously (IV) every six h), and metronidazole (500 mg IV every eight h) when he was admitted to our PICU. Human tetanus immune globulin (HTIG) was administered to the patient at the appropriate dose. He was monitored in a room in which reduced light and silence were provided in order to avoid triggering his symptoms. Because his muscle rigidity and spasms continued, diazepam (10 mg/dose in six doses), and baclofen (10 mg three times daily) were initiated. To suppress autonomic dysfunction and control spasms, a magnesium sulfate infusion was started. His clinical signs and laboratory results improved during follow-up. His muscle rigidity and spasms decreased and oral intake was increased. Serum levels of CK were normal. When his clinical signs improved, he was transferred from the PICU to the pediatric infectious disease ward.

After the patient's contractions decreased and his tachycardia regressed in the follow-up, magnesium sulfate infusion and diazepam were gradually discontinued. The dose of baclofen was reduced based on the recommendations of a pediatric neurologist. Penicillin and metronidazole therapy was completed in 14 days. He was discharged with a recommendation to be admitted to hospital for a follow-up.

The patient came for a reexamination after discharge, he had no health problems during the follow-up, and the physical examination was normal. A program for tetanus toxoid vaccination was arranged for the completion of a total of three doses.

LITERATURE REVIEW

To find the most comprehensive and updated recommendations for the prevention and treatment of tetanus, a targeted literature study was carried out. We looked for English-language articles published in the last ten years using the keywords "Tetanus" and "Pediatrics" in the databases of PubMed and Medline. Original studies and case reports were included. 22 articles comprising 146 pediatric cases are listed in Table 1[6-27]. The SPSS software (version 20, IBM, Armonk, New York, USA) was utilized for the statistical analysis of the studies included in the review. Descriptive statistics were used for the analysis of the data. According to the information provided, except for 12 patients diagnosed with otogenic tetanus, all 134 patients were unvaccinated or partially immunized. A total of 56 of the patients were diagnosed with neonatal tetanus. The neonate patients had history of unhealthy umbilical stump, lower abdominal septic skin infection, and post-circumcision infection. The other pediatric patients had history of trauma, lacerations, punctured injuries, and otogenic tetanus. All patients had typical symptoms of tetanus, such as lock-jaw, facial, abdominal muscle rigidity, painful neck stiffness, trismus, labile heart rate, tachypnea, hyperpyrexia, generalized spasms, risus sardonicus and opisthotonus. According to the data presented, among 146 pediatric patients with tetanus reported in the case series and studies in the literature, 41 (28%) of them died[6-27]. Our research has limitations such as the small sample size because it only covers the articles published in PubMed.

DISCUSSION

Generalized tetanus has become one of the forgotten infectious diseases thanks to universal vaccination with the tetanus toxoid[5]. Our case report and literature review is a reminder of this neglected disease and underline the significance of early clinical suspicion for tetanus, which has a fatal clinical picture among unvaccinated children. This case report may raise awareness of this vaccine-preventable illness, and it should be noted that early diagnosis can be vitally important.

Symptoms of tetanus can appear days to weeks after a wound[7]. This disease is typically accompanied by symptoms such as dysphagia, muscular spasms, and trismus of the head and neck[8]. Generalized tetanus may evolve to broad muscle stiffness and opisthotonus[23]. Muscle spasms can be very painful and are frequently triggered by stimulation[26]. Tachycardia, bradycardia, blood pressure changes and arrhythmias can all be symptoms of autonomic instability[17]. The spasms last for three to four weeks. A full recovery can take months[5,26].

Generalized tetanus should be considered in patients with a history of injury, painful muscle spasms and tonic contractions, trismus, opisthotonus, dysphagia, apnea due to upper airway obstruction, stiff neck, and symptoms of autonomic hyperactivity, who live in areas with low vaccination rates[1,5]. It's important to rule out other causes of spasms, such as hypocalcemia and drug or toxin intake[5].

Table 1 - Neonatal and pediatric cases diagnosed with tetanus in the literature.

Articles	Number of patients	Age	Inoculation site	Presenting symptoms	Vaccination history	Treatment	Outcome
Bagcı[6]	1 patient	16 months	Mucosal erosion in right cheek	Rigidity of jaw, face and neck, salivation	Unvaccinated	HTIG, penicillin, metronidazole, midazolam, tetanus toxoid vaccine	Survived
Ahmed *et al.*[7]	5 patients	3 years	Foot laceration	Fever, abdominal distention, and back pain	Unvaccinated	Exploratory laparotomy, HTIG tetanus toxoid vaccine metronidazole.	Survived
		7 years	Hand laceration	Trismus, jaw pain, and neck, back, and leg stiffness	Unvaccinated	HTIG, tetanus toxoid vaccine, penicillin	Survived
		11 years	Knee laceration	Trismus, pain, and discharge from wound	Unvaccinated	HTIG, tetanus toxoid vaccine, metronidazole cefazolin	Survived
		9 years	Foot splinter	Trismus and dysphagia	Unvaccinated	HTIG tetanus toxoid vaccine. metronidazole	Survived
		7 years	Foot laceration	Trismus, sore throat, and body stiffness	Unvaccinated	Magnesium sulfate, HTIG tetanus toxoid vaccine, metronidazole	Survived
Bagcı[8]	1 patient	9 years	Trunk injury	Chest, abdomen, back muscle stiffness	Unvaccinated	HTIG, tetanus toxoid vaccine. metronidazole, baclofen, midazolam, penicillin G	Survived
Cejudo-García de Alba *et al.*[9]	1 patient	6 years	Right arm splinter	Abdominal muscle stiffness, trismus difficulty walking	Incomplete immunization	Metronidazole, penicillin, wound debrided, HTIG tetanus toxoid vaccine	Survived
Asín *et al.*[10]	1 patient	7-day-old newborn	Umbilical cord	Muscular spasms, Trismus rigidity	Unvaccinated	HTIG, metronidazole diazepam, ampicillin gentamicin	Survived
Sesama *et al.*[11]	1 patient	7 years	Left ear discharge	Reflex spasm of masseters, left eye ptosis	Unvaccinated	Diazepam, ceftriaxone, metronidazole, supportive management, HTIG, diazepam	Survived
Akane *et al.*[12]	1 patient	13 years	Fracture of right distal radius	Trismus, muscle rigidity, excessive diaphoresis, risus sardonicus	Partially immunized	HTIG, tetanus toxoid, metronidazole, diazepam, penicillin G	Survived
Douvoyiannis *et al.*[13]	1 patient	9 years	Nail	Painful neck stiffness, lockjaw	Unvaccinated	HTIG, tetanus toxoid, midazolam	Survived
Homola *et al.*[14]	1 patient	2 and a half years	Deep erosion in the nasal mucosa, nasal toy	Difficulty swallowing trismus	Unvaccinated	Clindamycin, metronidazole, HTIG, tetanus toxoid	Survived
Condé *et al.*[15]	39 patients	13 days (median age)	Post-circumcision: 2 Umbilical cord: 20 Wound: 12 Limb fracture: 1	Fever, generalized muscle spasm, trismus	Unvaccinated: 17 Received 1 dose: 19 Received 2 doses: 3	NR	Died (n=20) Survived (n=19)
Maharaj *et al.*[16]	1 patient	1 week	Lower abdominal skin infection	NR	Unvaccinated	Sedatives, muscle relaxants, antibiotics, intrathecal / intramuscular immunoglobulin, wound treatment	Survived
Nakubulwa *et al.*[17]	1 patient	9 days	None	Labile heart rate, tachypnea, hyperpyrexia, abdominal muscle rigidity, generalized spasms	Maternal partially immunized	Cefotaxime, gentamicin, metronidazole, diazepam, magnesium sulfate, equine tetanus antitoxin	Survived
Okidi *et al.*[18]	1 patient	5-day-old neonate	NR	Fever, refusal to breastfeed, excessive crying, difficulty in breathing	Unvaccinated	Diazepam, metronidazole, phenobarbital	Died
Tadele *et al.*[19]	24 patients	8 years (median age)	Trauma Tungiasis	Generalized tetanus symptoms	Maternal partially immunized	Diazepam, chlorpromazine, debridement, penicillin G, metronidazole, tetanus toxoid	Survived (n=17) Died (n=7)

Table 1 - Neonatal and pediatric cases diagnosed with tetanus in the literature.

Articles	Number of patients	Age	Inoculation site	Presenting symptoms	Vaccination history	Treatment	Outcome
Ogunkeyede *et al.*[20]	23 patients	3.4 years	Otogenic tetanus	Ear discharge, trismus and spasms	Complete tetanus immunization (12), unvaccinated (6), partial tetanus immunized (5)	Topical antibiotic ear dressing, tetanus toxoid, HTIG, antibiotic therapy, sedatives	Died (n=3) Survived (n=20)
Barlas *et al.*[21]	2 patients	12 years	Puncture on right foot	Lock-jaw, facial, abdominal muscle rigidity	Unvaccinated	HTIG, tetanus toxoid, metronidazole, diazepam, vancomycin, ceftazidime, rocuronium, baclofen, fentanyl	Survived
		6 years	Puncture on left foot	Back pain, difficulty in opening the mouth and swallowing	Unvaccinated	ampicillin-sulbactam, metronidazole, HTIG, tetanus toxoid, fentanyl, baclofen, midazolam	Survived
Aqeel *et al.*[22]	30 patients	Neonate	Unhealthy umbilical stump	Muscle spasm, refusal to eat, abnormal posture	Maternal unvaccinated: 27 Maternal partially immunized: 3	HTIG, penicillin G, gentamicin, muscle relaxant pavulon	Died (n=6) Survived (n=24)
Irie *et al.*[23]	1 patient	2 years	Severe thermal burn	Fever, refusal to eat, trismus, generalized contractures	Unvaccinated	HTIG, amoxicillin clavulanic acid, benzodiazepine	Died
Neal *et al.*[24]	1 patient	10 years	Foot puncture	Muscle spasms, trismus, fever, risus sardonicus, opisthotonus	Unvaccinated	Diazepam, metronidazole, HTIG, tetanus toxoid, surgical debridement	Survived
Şık *et al.*[25]	1 patient	12 years	Right foot laceration	Spasms of the right foot, back, tachycardia hypertension, rigidity	Unvaccinated	Diazepam, morphine, vecuronium, magnesium sulfate, crystalline penicillin, HTIG, tetanus toxoid, intrathecal baclofen	Survived
Felter *et al.*[26]	1 patient	14 years	Right foot laceration	Speaking with difficulty, bilateral ptosis, pain, swelling, sternal chest pain with palpitations	Unvaccinated	Diazepam, lorazepam, HTIG, tetanus toxoid, metronidazole ciprofloxacin	Survived
Gowda *et al.*[27]	8 patients	Range: 2–11 years	Right foot laceration, left finger	Lock jaw, difficulty in walking	Unvaccinated: 6 Vaccinated: 2	Tetanus toxoid, crystalline penicillin, wound management care, HTIG	Survived (n= 5) Died (n= 3)

NR = not reported; HTIG = human tetanus immunoglobulin

Tetanus is more likely to spread to those with diabetes, dirt-contaminated wounds, older people, and injectable drug users[12].

Similarly to our patient, people who have never had an immunization are obviously at a greater risk for infection, but as anti-tetanus toxin antibody concentration declines with age, older adults are also at a higher risk of infection[12]. Tetanus in children is uncommon in developed countries. An anti-tetanus toxin antibody concentration of >0.01 IU/mL is typically regarded as the minimum protective threshold in modified enzyme-linked immunosorbent tests[12,28]. The degree of protective anti-tetanus toxin antibodies remains debatable[12]. Because tetanus immunity cannot be obtained spontaneously, it's crucial to receive all recommended vaccinations in pediatrics and maintain antibody levels throughout the course of life by receiving booster shots every 10 years[28]. Our patient's wounds were contaminated with dirt and we were unable to detect his antitoxin antibody concentration.

Conversely, some other reports in the literature claim that people with minor or subtle wounds may potentially contract a tetanus infection[12]. According to our literature review in Table 1, one pediatric patient who developed tetanus did not report an injury or wound[17].

Tetanus is treated by neutralizing residual tetanus toxoid antibodies, eliminating pathogens in the injured area, supportive care for respiratory failure, and controlling muscular spasm symptoms[29]. If left untreated, the case fatality rate is very high, almost 100%. Case mortality rates can decrease between 10% to 20% with appropriate therapy[5]. Pediatric intensive care is the cornerstone of management for generalized tetanus. To prevent triggering spasms, patients should be kept in quiet rooms with reduced light[8].

Benzodiazepines are preferred as therapies because they help to control rigidity and spasms, and provide a sedative effect[5]. An additional antispasmodic medication that reduces autonomic hyperactivity, and is also effective on spasms, is intravenous magnesium sulfate[29]. Other measures of tetanus management are active immunization and intramuscular injection of human TIG immediately after the diagnosis to prevent the worsening of the disease[5]. Human TIG neutralizes the unbound toxin[5,12]. Intramuscular or intravenous equine antitoxin is a suitable alternative if HTIG is not provided[17]. If equine antitoxin is used, skin testing should be done before giving the full dose to exclude hypersensitivity effects[29]. In a randomized controlled trial of 215 patients aged >16 years old, no advantage to using intramuscular human TIG (3,000 international units) in tetanus therapy versus intramuscular equine antitoxin (21,000 international units) was detected[30]. Intravenous immune globulin can be given if HTIG or equine antitoxin are not available[28]. To eliminate tetanus bacilli, antibiotics such as penicillin and metronidazole are recommended[29]. While *C. tetani* is often susceptible to penicillin, it has a weak infiltration into abscesses and can be neutralized by other microbial pathogens. Metronidazole was demonstrated to have excellent results in a controlled trial[26]. In several cases, surgical debridement is needed to eliminate spores and necrotic tissue that can provide a suitable environment for the further growth of spores[9].

Long-term functional results of the recovered patients from tetanus may be compromised and functional disabilities have been reported in the literature[31]. Tetanus-infected neonates may have neurological impairment, cognitive disability and cerebral palsy in long period follow-up[32].

It should be kept in mind that completing the full tetanus vaccination series during childhood, and maintaining immunity with tetanus booster shots during adulthood is essential and life-saving[28]. As seen in our review, this fatal disease (neonatal tetanus) still exists in areas where vaccination is not sufficient[22]. It is essential to vaccinate previously unvaccinated mothers in the prenatal period to prevent neonatal tetanus[33]. But even though the vaccine can be given at any stage during pregnancy, it is preferable for pregnant women to have the tetanus toxoid vaccination between 27 and 36 weeks of pregnancy[28]. Pregnant women who are partially immunized or unimmunized should take 3 vaccines containing tetanus toxoid within the indicated period[28,33]. If a previously unvaccinated pregnant woman takes at least two doses of the tetanus toxoid-containing vaccines at the recommended intervals, the probability of neonatal tetanus is minimal[28].

CONCLUSION

In conclusion, we described tetanus disease as observed in an unvaccinated adolescent. To enable early diagnosis of generalized tetanus because of its high fatality, it is crucial to obtain a detailed patient medical history and a comprehensive physical examination. Treatment of punctured, crushed, and traumatic injuries should be enhanced carefully to prevent tetanus[5]. Based on the fact that tetanus bacteria are always in the soil, this fatal disease cannot be eradicated but it can be reduced with increased tetanus vaccination worldwide[1,5]. Complete immunization is crucial because tetanus infection does not provide lifetime immunity to individuals who have had the disease[5].

CONFLICT OF INTERESTS

The authors report no conflict of interests.

FUNDING

None

REFERENCES

1. European Centre for Disease Prevention and Control. Disease factsheet about tetanus. [cited 2023 May 4]. Available from: https://www.ecdc.europa.eu/en/tetanus/facts
2. Blain A, Tiwari TS. Tetanus. In: Centers for Disease Control and Prevention. Manual for the surveillance of vaccine-preventable diseases. [cited 2023 May 4]. Available from: https://www.cdc.gov/vaccines/pubs/surv-manual/chpt16-tetanus.html
3. European Centre for Disease Prevention and Control. Tetanus: annual epidemiologic report for 2018. [cited 2023 May 4]. Available from: https://www.ecdc.europa.eu/en/publications-data/tetanus-annual-epidemiological-report-2018
4. World Health Organization. Tetanus reported cases and incidence. [cited 2023 May 4]. Available from: https://immunizationdata.who.int/pages/incidence/ttetanus.html
5. Rhinesmith E, Fu L. Tetanus disease, treatment, management. Pediatr Rev. 2018;39:430-2.
6. Bağcı Z. Cephalic tetanus: a rare case report. J Trop Pediatr. 2020;66:549-52.
7. Ahmed BS, Beck MJ, Williamson G, Ericson JE, Kumar P. Pediatric tetanus in Central Pennsylvania. J Pediatric Infect Dis Soc. 2019;8:358-60.
8. Bağcı Z. Truncal tetanus: a case report. J Trop Pediatr. 2021;67:fmaa129.
9. Cejudo-García de Alba MP, Valle-Leal JG, Sánchez Beltrán JG, Vázquez-Amparano AJ. Tetanus, a current disease in pediatric population: case report. Rev Chil Pediatr. 2017;88:507-10.

10. Pérez-Jacoiste Asín MA, Langbazounga M. Neonatal tetanus in an African newborn. Int J Infect Dis. 2018;67:1-2.
11. Sesama M, Gomber S, Yadav M. Cephalic tetanus presenting as ptosis. Indian Pediatr. 2020;57:72-3.
12. Akane Y, Tsugawa T, Hori T, Togashi A, Yoto Y, Inazawa N, et al. Tetanus in a partially immunized child. J Infect Chemother. 2018;24:980-2.
13. Douvoyiannis M, Belamarich PF, Goldman DL. Tetanus after vaccine refusal and an opportunity for the pediatric infectious diseases specialist. Clin Pediatr (Phila). 2015;54:513-6.
14. Homola L, Klučka J, Helešic J, Jirsenská Z, Kratochvíl M, Dominik P, et al. Unvaccinated child tetanus from nasal toy battery. Cent Eur J Public Health. 2021;29:322-4.
15. Condé I, Cherif MS, Dahal P, Hyjazi ME, Camara F, Diaby M, et al. Neonatal and postneonatal tetanus at a referral hospital in Kamsar, Guinea: a retrospective audit of paediatric records (2014-2018). Int Health. 2022;14:468-74.
16. Maharaj M, Dungwa N. Neonatal tetanus associated with skin infection. S Afr Med J. 2016;106:888-90.
17. Nakubulwa C, Opio E, Alekat GS, Kibetenga M, Alaroker FO. Neonatal tetanus with good outcomes at a regional referral hospital in Eastern Uganda: a case report. J Med Case Rep. 2022;16:54.
18. Okidi R, Sambo VD, Eyul J. Neonatal tetanus in St. Mary's Hospital Lacor: a case report. Clin Case Rep. 2020;8:2234-6.
19. Tadele H. Clinical profile and outcome of pediatrics tetanus: the experience of a tertiary hospital in Ethiopia. Ethiop J Health Sci. 2017;27:559-64.
20. Ogunkeyede SA, Daniel A, Ogundoyin O. Paediatric otogenic tetanus: an evidence of poor immunization in Nigeria. Pan Afr Med J. 2017;26:177.
21. Barlas ÜK, Kıhtır HS, Yeşilbaş O, Petmezci MT, Akçay N, Petmezci E, et al. Tetanus, a forgotten infection disease: a report of two cases. Turk J Pediatr. 2020;62:274-9.
22. Aqeel AY, Arishi HM, Ageel HI, Arishi NH. Epidemiological and clinical aspects of neonatal tetanus from a tertiary care hospital. Int J Pediatr Adolesc Med. 2017;4:71-4.
23. Irie BG, Asse KV, Kadiane NJ, Kofi N, Nda-Koffi C, Ogondon B, et al. Tetanus after application of traditional topical treatment to a severe burn. Med Sante Trop. 2018;28:446-7.
24. Neal M, Culbertson MC 3rd, Mendiratta S, Smith BC 3rd, Whittle JS. Boy with muscle spasms. Ann Emerg Med. 2017;70:432-40.
25. Şık G, Aydoseli A, Çıtak A. Intrathecal baclofen use in the management of tetanus related spasm: a case report. Turk J Pediatr. 2019;61:126-9.
26. Felter RA, Zinns LE. Cephalic tetanus in an immunized teenager: an unusual case report. Pediatr Emerg Care. 2015;31:511-3.
27. Gowda VK, Veerappa BG, Handral A, Benakappa A. Re-emergence of tetanus: epidemiological features, clinical profile and outcome from South India. Indian J Pediatr. 2016;83:1015-7.
28. Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, editors. Red book: 2021-2024 report of the Committee on Infectious Diseases. 32nd ed. Itasca: American Academy of Pediatrics; 2021.
29. Afshar M, Raju M, Ansell D, Bleck TP. Narrative review: tetanus - a health threat after natural disasters in developing countries. Ann Intern Med. 2011;154:329-35.
30. Van Hao N, Loan HT, Yen LM, Kestelyn E, Hong DD, Thuy DB, et al. Human versus equine intramuscular antitoxin, with or without human intrathecal antitoxin, for the treatment of adults with tetanus: a 2 × 2 factorial randomised controlled trial. Lancet Glob Health. 2022;10:e862-72.
31. Mahieu R, Reydel T, Maamar A, Tadié JM, Jamet A, Thille AW, et al. Admission of tetanus patients to the ICU: a retrospective multicentre study. Ann Intensive Care. 2017;7:112.
32. Barlow JL, Mung'Ala-Odera V, Gona J, Newton CR. Brain damage after neonatal tetanus in a rural Kenyan hospital. Trop Med Int Health. 2001;6:305-16.
33. Thwaites CL, Beeching NJ, Newton CR. Maternal and neonatal tetanus. Lancet. 2015;385:362-70.X